Nasopharyngeal Cancer Among Young People in the United States: Racial Variations by Cell Type [1]

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ABSTRACT—U. S. mortality and incidence statistics for nasopharyngeal cancer showed a fourfold excess risk of sarcomas in white children under age 10, and a fourfold to sevenfold excess of carcinomas in teen-age blacks. Mortality from nasopharyngeal carcinomas in young people was greater in the South than in the North, with the excess mortality in blacks linked to rural residence and low socioeconomic status. These and other characteristics of nasopharyngeal carcinoma in young persons suggested that environmental (perhaps infectious) agents are involved in this age group. These patterns contrasted with nasopharyngeal carcinomas developing after age 25, when the rates predominated in Chinese Americans. Nasopharyngeal cancer in the United States had three age peaks, with racial and epidemiologic distinctions that seemed to reflect different etiologies.—J Natl Cancer Inst 58: 1267-1270, 1977.

In the United States, susceptibility to nasopharyngeal cancer is elevated among Chinese Americans (*1*) and Alaskan natives (*2*). Racial differences have not been described for childhood occurrences of this tumor, although one might infer from recent clinical reports (*3–6*) that black children may be at increased risk. To further characterize nasopharyngeal cancer in childhood, a study was done with U.S. mortality and incidence statistics.

METHODS

The National Center for Health Statistics provided the NCI with copies of death certificates for all children under 15 years of age who died of cancer in the United States from 1960 to 1964, and for those under 20 years of age who died of cancer from 1965 to 1969 in all States except Missouri and Louisiana. Abstracted from the 144 death records for nasopharyngeal cancer were the child's age at death, race, sex, residence, tumor cell type, and associated diseases. Sib aggregation was evaluated by computer match of decedents' names, the names of parents, and residential address. Rates were calculated by race, sex, and 5-year age groups, with population estimates obtained by straight-line interpolation of census data for 1960 and 1970. To evaluate the effects of urbanization, race-specific mortality rates were calculated among counties grouped according to the proportion of residents living in rural areas, as reported in the 1960 census. SES was evaluated in a similar fashion, with the decedents' county of usual residence stratified by median years of school completed by the adult population. Additional mortality data covering all ages were obtained from the NCI survey of U. S. cancer mortality between 1950 and 1969 (*7*).

Incidence rates for nasopharyngeal cancer under age 20 were obtained from the Third National Cancer Survey, 1969–71 (*8*). Additional incident cases (not population based) were identified among children reported to the End Results Program of the NCI (*9*). This hospital-based tumor registry system has been used primarily to assess cancer survival rates.

The measure of the strength of an association was the RR, the ratio of the rate in one racial group to the rate in another. When we controlled for age, sex, urbanization, or SES, the measure used was the maximum likelihood estimate of RR obtained after stratification on the control variables (*10, 11*). The difference between the adjusted RR and 1.0 (no association) was tested for statistical significance by the method described by Mantel and Haenszel (*12*).

RESULTS

Mortality

The 144 childhood deaths from nasopharyngeal cancer, 1960–69, occurred among 108 whites and 36 nonwhites. All nonwhites in the series were black. Table 1 shows the sex- and race-specific death rates by histologic type and the age-specific death rates for sexes and races combined. Overall, there was a twofold excess risk of nasopharyngeal cancer in nonwhites compared to whites (RR controlled for age and sex=2.2; $P<0.001$). Analysis by histologic type revealed that nasopharyngeal *carcinoma* was 4½ times more common in nonwhites (RR=4.6; $P<0.001$). In contrast, nasopharyngeal *sarcoma* (70% classified as rhabdomyosarcomas) was 4½ times more common in whites (RR=4.4; $P<0.05$). In both races, tumors predominated in males (RR controlled for age and race=2.4: $P<0.01$). Carcinomas tended to develop in teen-agers, whereas sarcomas occurred earlier in childhood.

Text-figure 1 shows the age-specific mortality rates for nasopharyngeal cancer (data by histologic type were not available) in whites, blacks, and "other nonwhites" during the 20-year period, 1950–69. The age curve in whites was trimodal: 1) a small preadolescent mode consistent with the predominance of nasopharyngeal sarcoma in this group, 2) a second mode in the late teen-age years that levels off in young adults, and 3) a sharp increase after age 35 that plateaus later in life. The age curve for blacks was bimodal with a teen-age peak that is taller and more clearly defined than that in whites; later in life mortality was higher in blacks until surpassed at age 55 by the rates in whites. The rates for other nonwhites dominated the adult age range, and no teen-age peak was seen; only 2 deaths occurred under age 20 in this group. If the age-specific death rates for U. S. white children were applied to the number of Chinese Ameri-

ABBREVIATIONS USED: SES = socioeconomic status; RR = relative risk.

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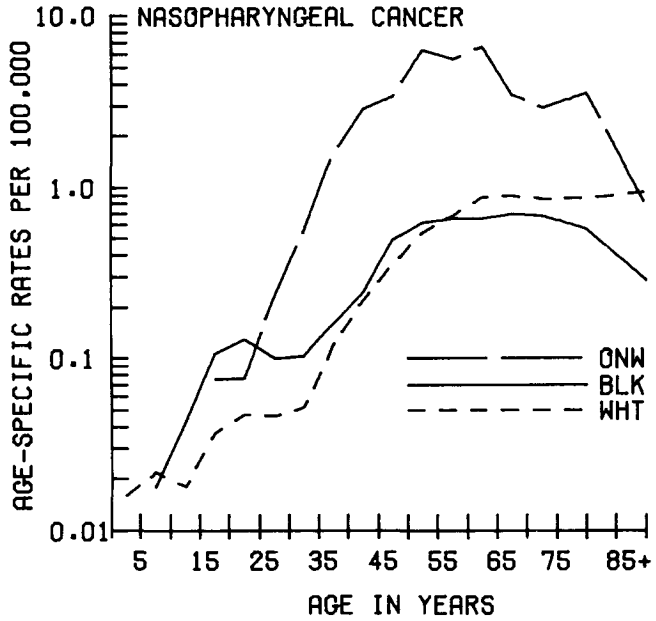
TABLE 1.—*Average annual death rates[a] (and No. of deaths) for nasopharyngeal cancer—childhood cancer mortality series, 1960–69:[b] Histologic type by age, race, and sex*

Tumor type	Total No.	Race and sex[c]				Age, yr			
		WM	WF	NM	NF	0–4	5–9	10–14	15–19[d]
Carcinoma	70	0.104 (29)	0.045 (12)	0.486 (22)	0.155 (7)	0.011 (2)	0.042 (8)	0.138 (25)	0.422 (35)
Sarcoma	57	0.136 (38)	0.063 (17)	0.022 (1)	0.022 (1)	0.070 (13)	0.143 (27)	0.066 (12)	0.060 (5)
Other and unspecified[e]	17	0.025 (7)	0.019 (5)	0.044 (2)	0.066 (3)	0.021 (4)	0.015 (3)	0.015 (3)	0.083 (7)
Total	144	0.265 (74)	0.127 (34)	0.552 (25)	0.243 (11)	0.102 (19)	0.200 (38)	0.219 (40)	0.565 (47)

[a] Crude rate (per million per yr).
[b] Louisiana, Missouri included for 1960–64 only.
[c] WM=white male, WF=white female, NM=nonwhite male, NF=nonwhite female.
[d] 1965–69 only.
[e] Lymphoma (2), teratoma (3), angiofibroma (1), malignant tumor not otherwise specified (11).



TEXT-FIGURE 1.—Age-specific mortality rates for nasopharyngeal cancer in the United States (1950–69) in whites (WHT), blacks (BLK), and other nonwhites (ONW). Deaths per 100,000. Source: (7).

can children at risk, 1950–69, one would expect 0.8 cases of nasopharyngeal cancer. If one applies the analogous rates from Hong Kong Chinese (*13*), one would expect 4.8 cases of nasopharyngeal cancer among Chinese American children. In fact, 1 case was observed.

Geographic analyses are presented in table 2. Mortality rates for nasopharyngeal carcinoma among nonwhites under age 20 were elevated in the East South Central and West South Central census divisions. The East South Central division also had the highest mortality rate for nasopharyngeal carcinoma among whites. The highest rate for nasopharyngeal sarcoma in whites was in the West South Central division.

The elevated nasopharyngeal cancer mortality rates in two Southern divisions suggested that the excess among blacks might be confounded by rural residence or low SES. Due to the rarity of sarcoma in nonwhites, further analysis was restricted to nasopharyngeal carcinoma. Counties of residence were ranked by proportion of rural residents and median number of school years completed, and the mortality rates were recalculated adjusting for each of these variables. The RR of nasopharyngeal carcinoma among nonwhites dropped from 4.6 to 2.9 when controlled for rural residence and to 2.5 when controlled for SES. Simultaneous control for both variables failed to yield a lower estimate of RR. These two variables were so highly correlated in our data that determining their independent effects was not possible.

No associated diagnoses were recorded on the death certificates of children with nasopharyngeal cancer. Also, no child with nasopharyngeal cancer had a sibling identified who died of any form of cancer during 1960–69.

Incidence

In the Third National Cancer Survey, 19 histologically verified cases of nasopharyngeal cancer were reported in patients under age 20. The 6 blacks in the survey had carcinomas (all after age 10), whereas 5 of the 13 whites had sarcomas (all prior to age 12). The incidence of nasopharyngeal carcinoma was 7 times higher in blacks than in whites (RR=7.1; $P<0.01$).

In the End Results series, there were 155 histologically verified cases of nasopharyngeal cancer in patients under age 20 (table 3). Although no population base is available, carcinomas represented 82% of all tumors in blacks and 61% of the tumors in whites. Given the presence of nasopharyngeal tumor, blacks were $4^1/_2$ times more likely than whites to develop a carcinoma ($P=0.05$). As in the other series, sarcomas tended to occur at an earlier age than did carcinomas.

DISCUSSION

The striking international and ethnic variations in nasopharyngeal cancer incidence have stimulated much etiologic research (*14*). However, the rarity of these tumors in Western countries requires large data resources to permit clarification of epidemiologic patterns by cell type, particularly in children. This study of death certificates and incidence data in the United States revealed a fourfold to sevenfold increased risk of nasopharyngeal carcinoma among nonwhites under age 20 compared to whites. The excess was confined to teenage blacks and was further evaluated in relation to published mortality statistics for nasopharyngeal cancer at

TABLE 2.—*Mortality rates[a] (and No. of deaths) for nasopharyngeal cancer by geographic region, race, and cell type—childhood cancer mortality series, 1960–69*

Census division	Nasopharyngeal carcinoma[b]		Nasopharyngeal sarcoma[b]	
	Whites	Nonwhites	Whites	Nonwhites
New England	0.114 (4)	—	0.142 (5)	—
Middle Atlantic	0.020 (2)	0.301 (4)	0.060 (6)	0.075 (1)
East North Central	0.067 (8)	0.350 (5)	0.109 (13)	—
West North Central	0.090 (4)	—	0.090 (4)	—
South Atlantic	0.111 (8)	0.302 (8)	0.125 (9)	—
East South Central	0.121 (4)	0.599 (7)	0.060 (2)	0.086 (1)
West South Central	0.085 (4)	0.486 (5)	0.169 (8)	—
Mountain	0.114 (3)	—	0.038 (1)	—
Pacific[c]	0.057 (4)	—	0.099 (7)	—
Total U.S.	0.075 (41)	0.320 (29)	0.100 (55)	0.022 (2)

[a] Crude rate (per million per yr).
[b] Dash indicates zero cases.
[c] Includes Alaska and Hawaii.

TABLE 3.—*No. of patients (%) under age 20 with nasopharyngeal cancer in the End Results series: Histologic type by age, race, and sex*

Tumor type	Total No.	Race and sex[a]				Age, yr			
		WM	WF	NM	NF	0–4	5–9	10–14	15–19
Carcinoma	104	49 (62)	20 (59)	20[b] (90)	15[c] (88)	3 (27)	4 (15)	30 (79)	67 (84)
Sarcoma	30	16 (20)	11 (32)	2 (8)	1 (6)	7 (64)	14 (54)	4 (10)	5 (6)
Other and unspecified[d]	21	14 (18)	3 (9)	3 (12)	1 (6)	1 (9)	8 (31)	4 (10)	8 (10)
Total	155	79 (100)	34 (100)	25 (100)	17 (100)	11 (100)	26 (100)	38 (99)[e]	80 (100)

[a] WM=white male, WF=white female, NM=nonwhite male, NF=nonwhite female.
[b] Seventeen blacks, 3 "other nonwhites."
[c] Fourteen blacks, 1 "other nonwhite."
[d] Lymphoma (13), malignant tumor not otherwise specified (8).
[e] Due to rounding off.

all ages. A trimodal age curve revealed: 1) a small peak under age 10 among whites only, resulting from the predisposition of this group to nasopharyngeal sarcomas, especially rhabdomyosarcoma [the predominance of the head and neck as a site for rhabdomyosarcoma in young children was described in (*15*)]; 2) a peak at 15–24 years, taller and more pronounced in blacks than in whites, and not evident in other nonwhites; 3) a larger peak in older adults, the rates being higher in blacks than whites until middle life and lower thereafter, with both curves overshadowed by the towering rates for other nonwhites [a reflection of the high mortality among Chinese (*1*)].

The geographic analysis of nasopharyngeal carcinoma under age 20 revealed elevated rates in the East South Central and West South Central census divisions of the United States. Further analyses suggested that rural residence and low SES may account for over half the excess mortality among black children. This is particularly striking in view of both incidence and mortality data suggesting that, in adults, nasopharyngeal carcinoma predominates in urban areas (*16, 17*).

Around the world, Chinese populations have the highest rates of nasopharyngeal carcinoma. The rates reported for young Chinese in Hong Kong (*13*) are higher than those for white and black children in the United States, but do not display the age peak at 15–24 years seen in U.S. mortality statistics for whites and blacks. Furthermore, only one death from nasopharyngeal cancer was reported in a Chinese American child between 1950 and 1969, compared with 4.8 expected on the basis of Hong Kong rates. Although small numbers are involved, the data are consistent with reports that the risk of nasopharyngeal cancer in Chinese Americans is lower among the U.S. born than in the foreign born (*18–20*). A postadolescent age peak has recently been observed in other parts of the world, including Tunisia (*21*) and India (*22*); this suggests etiologic heterogeneity of nasopharyngeal carcinoma in non-Chinese populations. In the United States, the excess risk in the young black population, together with a predominance of cases from rural and low SES background, suggests specific environmental factors, including oncogenic viruses (*14*). This latter possibility might be related to the tendency toward lymphocytic infiltration in nasopharyngeal carcinomas in young people, often described as "lymphoepitheliomas" (*5*). In addition, review of the literature revealed 12 non-Oriental families prone to nasopharyngeal carcinoma (*4, 23–25*). Age at diagnosis was recorded for 11 families, 8 of which had all cases under age 25; this suggests that familial susceptibility may also be a characteristic of the "early peak" of nasopharyngeal carcinoma.

The multimodal age curve associated with various risk factors and histologic patterns resembles that described for Hodgkin's disease by MacMahon (*26*), who postulated an infectious etiology for the "young adult" peak. Investigators pursuing the possible viral origin of nasopharyngeal carcinoma may find it profitable to direct their attention to teen-age and young adult patients.

The age and race patterns of nasopharyngeal cancer suggest etiologic heterogeneity which should be taken into account in further laboratory and epidemiologic studies of these tumors.

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